Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Microbiology and Infection 27 (2021) 1570–1574

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Commentary

COVID-19 vaccination in Israel

Khitam Muhsen*, Dani Cohen

Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ARTICLE INFO

Article history:
Received 12 June 2021
Received in revised form
26 July 2021
Accepted 31 July 2021
Available online 9 August 2021

Editor: L. Leibovici

Keywords:
BNT162b2 COVID-19 vaccine
COVID-19
Israel
mRNA vaccines
Vaccine effectiveness

Introduction

Initial reports on the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the aetiological cause of coronavirus disease 2019 (COVID-19), were published in December 2019. Since then, COVID-19 has resulted in substantial morbidity and mortality globally [1]. From December 2020 through the beginning of 2021, several COVID-19 vaccines received regulatory authorization in many countries.

The population of Israel includes more than nine million people. Approximately 74% are Jews (of which nearly 12% are ultraorthodox (religious)), 21% are Arabs and 5% are of other religions and ethnicities [2]. The healthcare system in Israel is characterized by universal health insurance. Under the regulation of the Ministry of Health (MoH), a broad basket of health services is provided to all citizens through four health maintenance organizations (sick funds). Each citizen must be a member of one of these sick funds that supply primary care services via community clinics. Inpatient services are generally provided by public hospitals, with associated costs covered by the sick funds [3]. All sick funds maintain electronic health records and have well developed physical and virtual infrastructure and paths of communication with their members.

Centralized management of the COVID-19 epidemic in Israel was led by the MoH, and operationalized by sick funds and hospitals. Operational assistance was provided by the military, civilian organizations, and local municipalities.

Before COVID-19 vaccines became available, non-pharmaceutical preventive measures were implemented in Israel to control the epidemic, including limitations on international travel, school closures, social and physical distancing, obligatory face masks in public spaces (enforced by law), cancellation of mass gatherings, and several prolonged near-complete lockdowns [4]. In addition, a large-scale programme of contact tracing and isolation was implemented through epidemiological investigations and digital tracking, with widespread RT-PCR testing among contacts of confirmed COVID-19 patients [4]. These measures were associated with a reduced risk of SARS-CoV-2 transmission [5]. Nonetheless, maintaining strict public compliance with non-pharmaceutical preventive measures was challenging, and disease surges that occurred after lockdowns were lifted suggested that such measures may be effective only for short-term reduction of viral transmission and disease burden. On 19th December 2020, Israel introduced mass vaccination with the BNT162b2 mRNA vaccine (Pfizer-BioNTech) [6]. Herein we describe the Israeli experience and perspective on COVID-19 immunization.

COVID-19 vaccine introduction and deployment

The BNT162b2 COVID-19 vaccine was introduced in Israel during a third nationwide wave of COVID-19 infections, and while under lockdown (Fig. 1). Vaccine introduction was accompanied by an extensive campaign which was entitled ‘Back to Life’ to encourage vaccine uptake. Positive incentives, termed ‘the green passport’ (also known green tag), were provided to immunized individuals that allowed them to attend events with larger gatherings such as theatres, restaurants and hotels.

Initially, healthcare workers, individuals aged ≥60 years, and those with underlying diseases were prioritized for COVID-19 immunization, after which the vaccine was offered to residents aged ≥16 years in a staggered, age-descending manner. At the beginning of June 2021, Israel's MoH approved the BNT162b2 vaccine for use

* Corresponding author. Khitam Muhsen, Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University Ramat Aviv, Tel Aviv 6139001, Israel.
E-mail address: kmuhsen@tauex.tau.ac.il (K. Muhsen).

https://doi.org/10.1016/j.cmi.2021.07.041

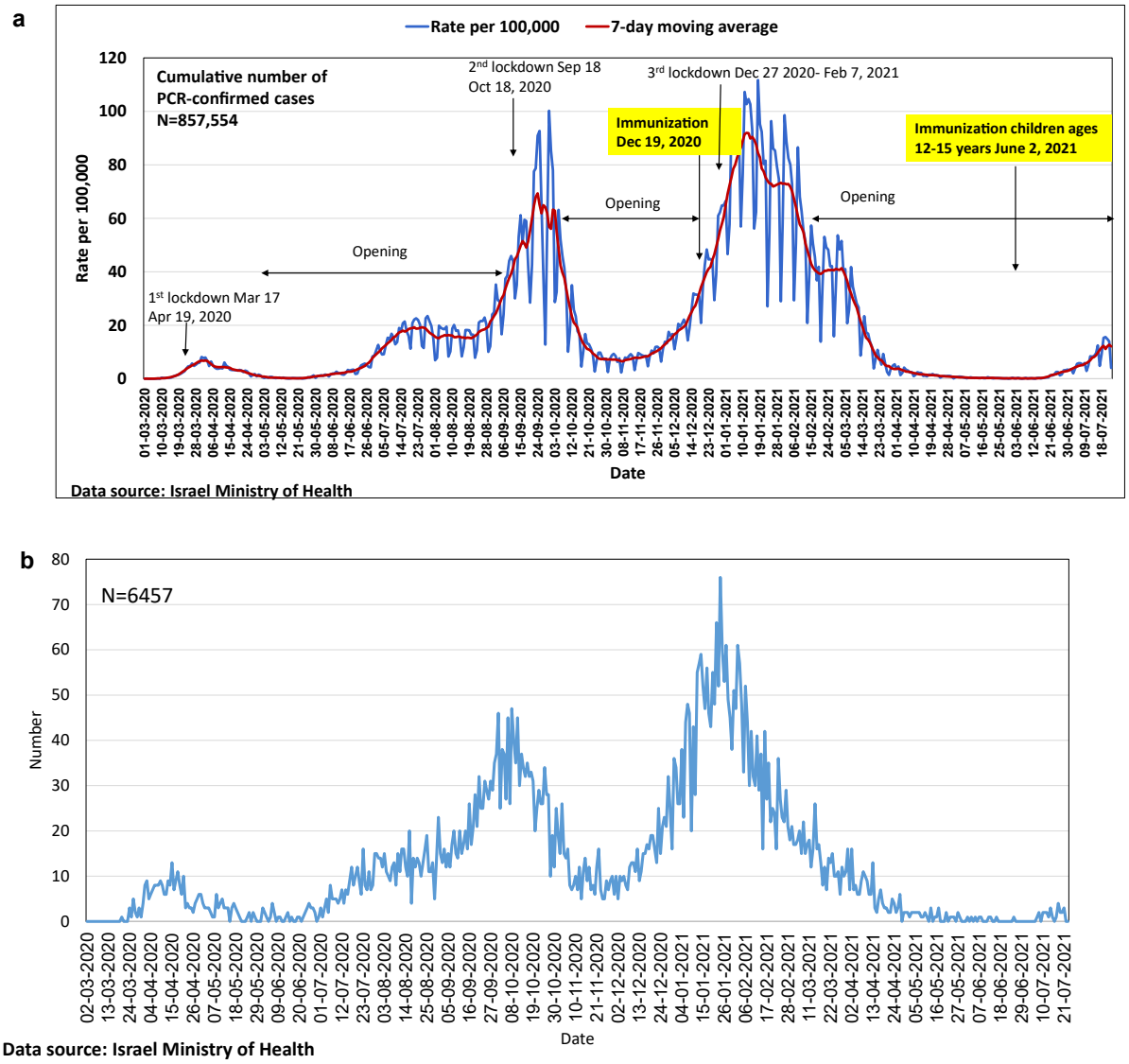

Fig. 1. (a) Incidence rate of RT-PCR-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, Israel March2020–July 2021. (b) Coronavirus disease 2019 (COVID-19)-related deaths, Israel March 2020–July 2021.

among 12–15-year-old adolescents. The vaccine is given in two doses, 3 weeks apart.

Vaccinations were provided by the four sick funds, each of which established immunization centres/clinics across the country. Support was provided by the Home Front Command, emergency care providers such as Magen David Adom, and local municipalities to optimize reach in remote areas and for prioritized populations such as nursing-home residents [4]. Special government funding for vaccine purchasing, timely negotiations and contracts with vaccine manufacturers for a large supply of vaccines relative to Israel's population, well-developed information technology and logistical capacities of the community-based sick funds, and coordination with the MoH, medical centres and emergency care providers were leading factors contributing to the successful deployment of the COVID-19 vaccination in Israel (10).

Vaccine uptake

Vaccine uptake was rapid (Fig. 2a), and within 2 months about half of the total population had received a vaccine dose. As of 1st June 2021, 81% of the population aged ≥16 years had received the second vaccine dose. Vaccine uptake was high, exceeding 75% among those aged 20 years and increasing with age, surpassing 90% in individuals aged ≥60 years (Fig. 2b).

Potential explanations for the rapid rollout and uptake of COVID-19 vaccine in Israel

Multiple factors likely contributed synergistically to the rapid uptake of the COVID-19 vaccine in Israel, including factors related to preparedness and management of COVID-19 vaccination and general characteristics of the country and healthcare system as described above [10]. The government's high commitment and trust in vaccines as a solution for the COVID-19 crisis was declared by the Prime Minister very early in 2020 and was translated into allocation of funds and efforts for purchasing vaccines early and towards successful distribution of the vaccines. The government also funded development of a COVID-19 vaccine in Israel, Brilife, a viral vector-based vaccine, which is currently in phase I/II clinical trials [11].

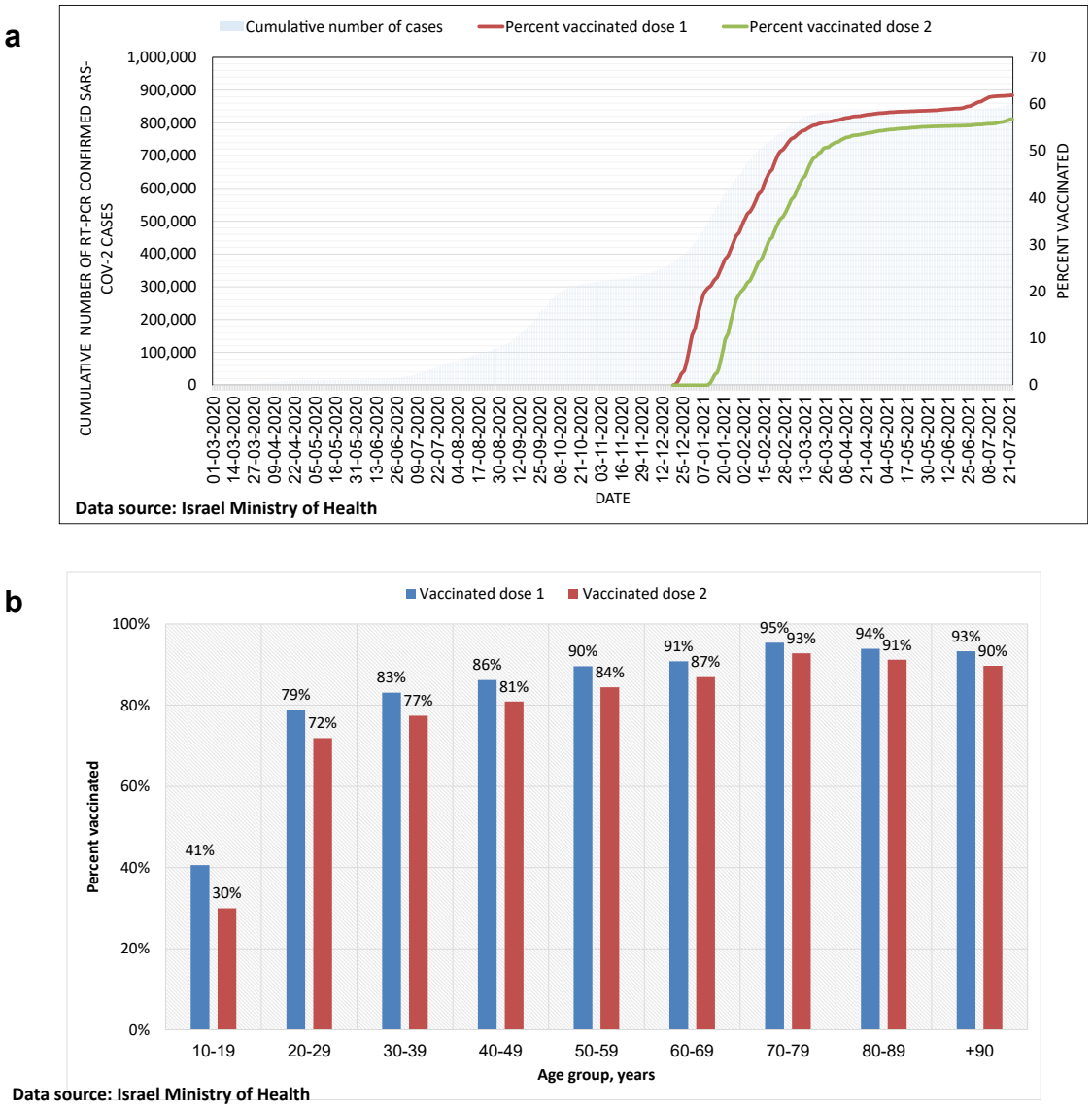

Fig. 2. (a) Cumulative number of RT PCR-confirmed cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and uptake of coronavirus disease 2019 (COVID-19) vaccine in Israel. (b) COVID-19 vaccine uptake by age and vaccine dose, Israel.

At the preparedness stage, in early 2020 the MoH was in contact with multiple vaccine manufacturers that were working on development of COVID-19 vaccines to ensure availability of sufficient vaccine doses as quickly as possible. Upfront, the government purchased enough vaccine doses with which to immunize all people aged ≥16 years. These efforts proved successful, as shortly after the Food and Drug Administration (FDA) authorization of the BNT162b2 vaccine, initial shipments of the vaccine doses arrived in Israel. Storage warehousing with adequate cold conditions (−70°C) could be prepared in advance due to the existing physical and operational infrastructure. COVID-19 immunization priorities and timelines were clear, and determined in advance by the MoH in consultation with specific committees of experts.

Implementation of the COVID-19 immunization campaign in the general population was run by the four sick funds; each quickly established designated call centres and computerized systems to make vaccination appointments at immunization centres distributed across the country, extended opening hours (including over weekends), and trained nurses and medical personnel. The available expertise of the sick funds alongside the relatively small geographical and population size likely contributed significantly to the rapid establishment and efficient organization of these centres.

COVID-19 immunization was accompanied by well-designed mass advertising campaigns, in mass media, across social media platforms, and in multiple languages. These campaigns included simple messaging and provided reliable information on vaccine safety and efficacy, which are critical elements for addressing vaccine hesitancy and related concerns.

Documentation of immunization in electronic health records was done immediately after administration of the vaccine, which enabled real-life monitoring of vaccine uptake nationally and within local municipalities. Immunization data from all sick funds became available immediately in a national MoH database and served as a basis for decision-making. For example, high demand for the vaccine led to increasing numbers of immunization centres.

Initially, vaccine uptake was slower and lower in the Arab and ultraorthodox (religious) Jewish populations than in the general Jewish population [4,12]. However, following culturally tailored

interventions undertaken by the MoH, sick funds and local stakeholders, these gaps were reduced, although not fully eliminated. Interventions included engagement of, and working closely with, the local municipalities and community leaders (e.g. religious leaders, medical personnel), who became an integral part of decision-making and operation of the immunization distribution. Moreover, advertising of COVID-19 immunization was refined to meet the needs and concerns of the Arab and ultraorthodox communities by using tailored language and adapting approaches to cultural motives of the population. Additional immunization centres, including mobile clinics, were also opened to enhance access to vaccines in these populations and in remote regions.

Immunization of special groups such healthcare workers was undertaken by the employing medical centres at the first phase of COVID-19 immunization. Thus, being the first to get the vaccine, medical personnel served as role models for the general population in accepting COVID-19 vaccination. This, coupled with the positive incentives given to vaccinees (i.e. green passport [tag]), likely encouraged people to get vaccinated. Immunization of residents of nursing homes and long-term care facilities was undertaken in the framework of a 'Senior Shield' programme with designated funding and resources; this was completed towards the end of January 2021, thus providing protection rapidly to this vulnerable population, and freeing personnel to complete immunization of the general population.

Collectively, these factors led to high and rapid uptake of COVID-19 vaccines in Israel.

BNT162b2 vaccine effectiveness and impact

While the BNT162b2 vaccine showed 95% efficacy against COVID-19 in a phase III trial [6], assessment of vaccine effectiveness in real life was needed. The availability of electronic medical records in Israel facilitated the conduct of such rapid assessments [7–9,13]. A nationwide analysis up to April 2021 showed vaccine effectiveness estimates at ≥7 days after the second dose of 91.5% against asymptomatic SARS-CoV-2 infection, and 97.0% against symptomatic infection, COVID-19 hospitalizations, severe disease and death, during a period in which the variant of concern, α (B.1.1.7), was predominant in Israel [8]. Further studies are needed to assess the vaccine effectiveness against additional emerging variants of concern, i.e. β (B.1.351), γ (P.1) and δ(B.1.617.2).

Testing for SARS-CoV-2 mostly relied on self or physician referral, which might be affected by immunization status. Furthermore, vaccinated and unvaccinated individuals likely differ in health behaviours and other characteristics. Under the circumstances of high vaccination coverage, unvaccinated persons likely represent marginal population segments that decline vaccination for various reasons. Studies undertaken by Chodick et al. addressed these shortcomings [7,13].

Based on the results of a phase III trial [6], the BNT162b2 vaccine did not induce protection until day 12 following immunization with the first dose; this period can therefore be used as a reference when comparing the incidence of infection after day 7 following immunization with the second dose [7]. Using this method, Chodick et al. showed vaccine effectiveness of 94% against COVID-19, which was consistent across age, sex and population groups, although effectiveness was lower among immunosuppressed patients [7]. Another study from Israel showed that immunization of pregnant women with the BNT162b2 vaccine was safe and effective against SARS-CoV-2 infection [14].

The quick and high uptake of the second vaccine dose coupled with the high effectiveness against SARS-CoV-2 infection and COVID-19 led to substantial and consistent reduction in COVID-19 incidence and mortality [4,8]. These encouraging decreases were followed by gradual reopening and lifting of COVID-19 restrictions. This corresponds to sustained declines in COVID-19 incidence in all age groups, including unvaccinated age groups, thus suggesting indirect protection (herd immunity) conferred by BNT162b2. Herd immunity was also built upon the increasing number of persons who had recovered from COVID-19, from 432 063 at the beginning of January 2021 to 782 335 at the beginning of March 2021, reaching 857 554 towards the end of July 2021. The number of persons with natural undetected SARS-CoV-2 infection is likely greater by a factor of 4–15 as demonstrated in a nationwide seroepidemiological study [15]. Israel's MoH recommends immunization with a single dose of BNT162b2 for individuals who recovered from COVID-19 at least 3 months after recovery. It is estimated that 20–25% of those who recovered from COVID-19 received BNT162b2 vaccine; this likely also enhanced the development of herd immunity.

Towards the end of June and at the beginning of July 2021 a consistent increase in the incidence of SARS-CoV-2 infection has been seen (Fig. 1), including among vaccinated persons, with most infections caused by the δ variant of concern.

BNT162b2 vaccine safety

An analysis of reports of events that occurred within 30 days following immunization of 5.4 million people with the first dose and 5.09 million people with second dose suggests that overall the vaccine had a safe profile, with the majority of adverse events being mild and transient; these events included both systemic (weakness, headache, fever) and local (pain, erythema) reactions [16]. According to an MoH press release on 1st June 2021, 148 people developed myocarditis after immunization with the BNT162b2 vaccine, usually shortly after receiving the second vaccine dose. Most of these cases were young males. The illness was described as mild in most cases, with the exception of one fatal case. It was concluded that immunization with BNT162b2 was positively related to the occurrence of these cases [16] (MoH Telegram). The occurrence of myocarditis following immunization with both mRNA vaccines BNT162b2 and mRNA-1273 (Moderna) was reported in the United States and Europe, and a few case series were published from Israel [17–22]. The FDA's emergency use authorization has been modified to include information on myocarditis risk after the receipt of mRNA COVID-19 vaccines [20].

Immunization of children and adolescents aged 12–15 years

Following the FDA authorization of the BNT162b2 vaccine among children aged 12–15 years, Israel's MoH recommended immunization of this age group. About 2 months after the MoH's recommendation, vaccine uptake among children aged 12–15 years remains low at around 30%.

Conclusions

The deployment of the COVID-19 vaccine in Israel was rapid and successful due to well organized national efforts of all health sectors in the country, the existing infrastructure, and the allocation of adequate resources. This was reflected by high uptake of both vaccine doses, increased vaccine compliance among the ultraorthodox Jewish population and Arab populations, high vaccine effectiveness, and consistent and sustained declines in COVID-19 incidence and mortality which eventually achieved the goal of the 'Back to Life' campaign. Remaining challenges include: (a) maintaining this success, especially with the removal of nearly all COVID-19 restrictions and alongside a current increase in disease incidence throughout July 2021, (b) increasing vaccine uptake

among adolescents aged 12–15 years, (c) reducing the remaining gaps in COVID-19 vaccine uptake across specific population groups (Arabs and ultraorthodox Jews relative to the general Jewish population), and (d) understanding the duration of protection conferred by the BNT162b2 vaccine and protection against new SARS CoV-2 variants of concern.

Authors contributions

KM and DC designed the manuscript sections and content. KM prepared the figures and wrote the first draft of the manuscript. DC reviewed the manuscript critically and contributed to writing. Both authors approved the manuscript.

Transparency declaration

The authors declare no conflicts of interest. No external funding was available for this work.

References

[1] WHO. Coronavirus disease (COVID-19) pandemic. 2020. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019.
[2] Internet Population of Israel on the Eve of 2021—9.3 million. Israel Central Bureau of Statistics; 2020. Available from: https://www.cbs.gov.il/he/mediarelease/Pages/2020/%D7%90%D7%95%D7%9B%D7%9C%D7%95%D7%A1%D7%99%D7%99%D7%AA-%D7%99%D7%A9%D7%A8%D7%90%D7%9C-%D7%91%D7%A4%D7%AA%D7%97%D7%94-%D7%A9%D7%9C-%D7%A9%D7%A0%D7%AA-2021-.aspx.
[3] Clarfield AM, Manor O, Nun GB, Shvarts S, Azzam ZS, Afek A, et al. Health and health care in Israel: an introduction. Lancet 2017;389:2503–13.
[4] Muhsen K, Na'aminh W, Lapidot Y, Goren S, Amir Y, Perlman S, et al. A nationwide analysis of population group differences in the COVID-19 epidemic in Israel, February 2020–February 2021. Lancet Reg Heal Eur 2021;7:100130.
[5] Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schunemann HJ, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. Lancet 2020;395:1973–87.
[6] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. New Engl J Med 2020;383:2603–15.
[7] Chodick G, Tene L, Rotem RS, Patalon T, Gazit S, Ben-Tov A, et al. The effectiveness of the two-dose BNT162b2 vaccine: analysis of real-world data. Clin Infect Dis 2021:ciab438.
[8] Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. Lancet 2021;397:1819–29.
[9] Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. New Engl J Med 2021;384:1412–23.
[10] Rosen B, Waitzberg R, Israeli A. Israel's rapid rollout of vaccinations for COVID-19. Isr J Health Policy Res 2021;10:6.
[11] Israeli COVID-19 vaccine developer inks deal to complete trials. 2021. Available from: https://nocamels.com/2021/07/israeli-covid-19-vaccine-brilife-trials-jab/.
[12] Ber I, Lerman Y, Muhsen K. The need for reducing disparities in SARS-CoV-2 immunization: the ultraorthodox and Arab populations in Israel. Harefuah 2021;160:285–90.
[13] Chodick G, Tene L, Patalon T, Gazit S, Ben Tov A, Cohen D, et al. Assessment of effectiveness of 1 dose of BNT162b2 vaccine for SARS-CoV-2 infection 13 to 24 days after immunization. JAMA Netw Open 2021;4:e2115985.
[14] Goldshtein I, Nevo D, Steinberg DM, Rotem RS, Gorfine M, Chodick G, et al. Association between BNT162b2 vaccination and incidence of SARS-CoV-2 infection in pregnant women. JAMA 2021:e2111035.
[15] Reicher S, Ratzon R, Ben-Sahar S, Hermoni-Alon S, Mossinson D, Shenhar Y, et al. Nationwide seroprevalence of antibodies against SARS-CoV-2 in Israel. Eur J Epidemiol 2021:1–8.
[16] MOH. Adverse events occurring shortly after immunization. Internet. Israel Ministry of Health; 2021. Available from: https://www.gov.il/BlobFolder/reports/vaccine-efficacy-safety-follow-up-committee/he/files_publications_corona_side-effects-after-vaccination-30042021.pdf.
[17] CDC. Myocarditis and pericarditis following mRNA COVID-19 vaccination. Internet. 2021. Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html.
[18] EMA. COVID-19 vaccines: update on ongoing evaluation of myocarditis and pericarditis. Internet. 2021. Available from: https://www.ema.europa.eu/en/news/covid-19-vaccines-update-ongoing-evaluation-myocarditis-pericarditis.
[19] Snapiri O, Rosenberg Danziger C, Shirman N, Weissbach A, Lowenthal A, Ayalon I, et al. Transient cardiac injury in adolescents receiving the BNT162b2 mRNA COVID-19 vaccine. Pediatr Infect Dis J 2021. https://doi.org/10.1097/INF.0000000000003235 (online ahead of print).
[20] Gargano JW, Wallace M, Hadler SC, Langley G, Su JR, Oster ME, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: update from the Advisory Committee on Immunization Practices—United States, June 2021. MMWR Morb Mortal Wkly Rep 2021;70:977–82.
[21] Montgomery J, Ryan M, Engler R, Hoffman D, McClenathan B, Collins L, et al. Myocarditis following immunization with mRNA COVID-19 vaccines in members of the US military. JAMA Cardiol 2021. https://doi.org/10.1001/jamacardio.2021.2833.
[22] Abu Mouch S, Roguin A, Hellou E, Ishai A, Shoshan U, Mahamid L, et al. Myocarditis following COVID-19 mRNA vaccination. Vaccine 2021;39:3790–3.